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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/657,986	09/08/2000	Edwin L. Madison	225/049	2665

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EXAMINER

WALICKA, MALGORZATA A

ART UNIT	PAPER NUMBER
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1652

DATE MAILED: 07/30/2002

18

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/657,986

Applicant(s)

MADISON ET AL.

Examiner

Malgorzata A. Walicka

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on 04 June 2002.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-15 is/are pending in the application.
- 4a) Of the above claim(s) 6 and 8-15 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-5 is/are rejected.
- 7) ☒ Claim(s) 7 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892) 4) ☐ Interview Summary (PTO-413) Paper No(s). _____
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948) 5) ☐ Notice of Informal Patent Application (PTO-152)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ 6) ☐ Other: _____

The Response under 37 CFR § 1.111, filed on June 4, 2002 as paper No. 17 is acknowledged. Claims 1-15 are pending in the application. Claims 1-5 and 7 are elected by Applicants, and are the subject of this Office action. Claims 6, and 8-15 are withdrawn from consideration as drawn to the non-elected invention.

OFFICE ACTION

1. Restriction/election

The examiner acknowledges the election, with traverse, of the compound No. 4 in Fig. 1A for examination on merits. Applicants request that the scope of examination be increased to include the genus upon finding of ~~an~~ allowable species.

Applicants reiterate their traverse of restriction requirement as set forth in their response of November 30, 2001, and request that Group II and I be combined for prosecution because they are properly examinable together without undue burden on examiner. This is not found persuasive because while the searches for the two Groups overlap, they are not coextensive. The search for Group I would require the search of classes and subclasses unnecessary for the search of elected Group II. For example, search of Group I would require search of class 514, subclass 2, which is not required for Group II, classified in class 435, subclass 23.

In addition, Group I and II are patentably distinct for reasons set forth in the restriction requirement, paper No. 7.

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In conclusion, the requirement is still deemed proper and is therefore made FINAL.

2. Objections

2.1. Specification

The specification is objected to because Figure 1C and Table 1 are missing from the specification.

2.2. Claims

Claim 7 is objected to because the structure of compound No.4 in Fig.1 is missing in the claim. Where possible, claims are to be complete in themselves. Incorporation by reference to a specific figure or table "is permitted only in exceptional circumstances where there is no practical way to define the invention in words and where it is more concise to incorporate by reference than duplication a drawing or table into claim. Incorporation by reference is a necessity doctrine, not for applicant's convenience." *Ex parte Fressola*, 27 USPQ2d 1608, 1609 (Bd. Pat. App. & Inter. 1993)." (citations omitted)

3. Rejections

3.1. 35 USC, section 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 1-5 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The claims recite the abbreviation MTSP1 that should be expanded.

Due to lack of Figure 1C in the specification claim ³4 is rejected as incomplete.

3.2. 35 USC, section 112, first paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3.2.1. Rejection for lack of written description

Claim 1-5 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims recite a large and variable genus of chemical compounds that are inhibitors of serine proteases. The serine protease inhibitors belong to different types of chemicals. Only protein inhibitors are classified into 10 families. Current publications, see the enclosed form PTO 982, disclose several inhibitors of matriptase that are proteins or non-proteins type. The specification discloses only a few representative compounds of the genus. Teaching the structure of only a few inhibitors of matriptase is

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not sufficient to provide specific characteristic of the genus. Therefore, one skilled in the art is not convinced that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In addition, the claims and the specification fail to describe any inhibitor that has an IC_{50} of 100 nM or less, because Table 1 that should, according to the text on page 33, line 30, present IC_{50} values of the disclosed compounds is missing from the specification.

3.3. Rejection for scope of enablement

Claims 1 to 5 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of treating with the compound No. 4, does not reasonably provide enablement for treatment with any inhibitor of serine protease activity of matriptase or MTSP1. In addition, claims 2 and 5 are directed to the method of treatment with an inhibitor wherein the inhibitor's IC_{50} is of 100 nM or less. The specification is silent about an inhibitor having IC_{50} that is of 100 nM or less; see the above rejection for lack of written description.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims. The claims are directed to any inhibitor of serine protease activity, i.e. to a large and variable genus of chemical compounds or to any inhibitor having IC_{50} of 100 nM or less.

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The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of inhibitors of serine protease activity that are broadly encompassed by the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)), otherwise the experimentation left to those of skill in the art is undue.

Factors to be considered in determining whether undue experimentation is required, are summarized *In re Wands* [858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)]. The Wands factors are: (a) the quantity of experimentation necessary, (b) the amount of direction or guidance presented, (c) the presence or absence of working example, (d) the nature of the invention, (e) the state of the prior art, (f) the relative skill of those in the art, (g) the predictability or unpredictability of the art, and (h) the breadth of the claim.

The nature and breadth of the claimed invention encompasses any compound which inhibits serine protease activity of matriptase or MTSP1 or any inhibitor having IC_{50} of 100 nM or less.

The claimed genus of the compounds is a large and variable genus of serine protease inhibitors; see the above rejection for lack of written description. The specification only discloses the structure of its single representative, compound No. 4 in Fig. 1A. In addition, the specification fails to teach any data for IC_{50} of disclosed compounds.

Although chemical synthesis of serine protease inhibitors is a vividly developing art, and skills of artisans high, it is not a routine experimentation in the art to synthesize

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and screen all possible compounds for those that inhibit, or selectively inhibit, serine protease activity of matriptase or MTSP1. In addition, in case of claims 2 and 5 the experimentation would require examination of IC_{50} , and selecting those compounds having IC_{50} that is of 100 nM or less. The probability of making the claimed invention is low. One skilled in the art is unable to make the claimed invention without guidance on the part of Applicants as to the structure of the recited inhibitor. Without the further guidance the experimentation left to those skilled in the art is unnecessarily and improperly extensive and undue.

4. Conclusion

The application contains allowable subject matter. Claim 7 would be allowed if not for formal requirements indicated in paragraph 2.2 of this Office action. The following is a statement of reasons for the indication of allowable subject matter: applicants disclose a unique chemical compound that is a new inhibitor of the serine domain of matriptase. The compound has a potential use in treatment of cancerous conditions, to decrease tumor growth and to retard metastasis.*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Malgorzata A. Walicka, Ph.D., whose telephone number is (703) 305-7270. The examiner can normally be reached Monday-Friday from 10:00 a.m. to 4:30 p.m.

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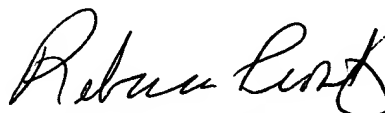
If attempts to reach examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapura Achutamurthy, Ph.D. can be reached on (703) 308-3804. The fax number for this Group is (703) 305-3014.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionists whose telephone number is (703) 308-0196.

Malgorzata A. Walicka, Ph.D.

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Patent Examiner


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